PROUT (T. P.)

SOME MINOR STUDIES IN NERVE CELL DEGENERATION AS PRESENTED BY A CASE OF LOCALIZED CEREBRAL ATROPHY.

THOMAS P. PROUT, M. D.,

STATE HOSPITAL, MORRIS PLAINS, N. J.

Reprinted from the American Journal of Insanity, for April, 1895.

SOME MINOR STUDIES IN NERVE CELL DEGENERATION AS PRESENTED BY A CASE OF LOCALIZED CEREBRAL ATROPHY.

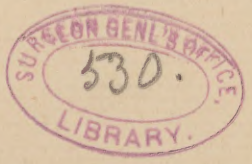
BY THOMAS P. PROUT, M. D.,
Assistant Physician and Pathologist to the New Jersey State Hospital at Morris Plains.

The case, P. C. H., age forty, admitted to the New Jersey State Hospital at Morris Plains, July 28, 1892, was that of an epileptic of nine years standing at the time of his admission. His epileptic seizures were of very severe nature, but general in character, occurring at long intervals and with unfailing regularity up to the time of his death, which took place on the morning of November 22, 1894. He died during a severe epileptic seizure.

The autopsy showed a condition of considerable interest, from the records of which the following is an abstract: The dura mater presented on the left side several irregular calcareous plates varying in size, but covering a considerable portion of that side of the brain. In the circle of Willis there was no posterior communicating artery found on the right side. There was marked difference in the size of the two hemispheres, the left being much the smaller and also much contracted anteriorly and posteriorly. Certain of the convolutions over the whole brain surface, but especially on the left side, seemed almost obliterated. These atrophied areas involved especially the convolutions of the left occipital region and a smaller portion of the frontal areas of both sides, with markedly atrophied areas of less extent in other portions of the brain. The motor areas remained uninvolved. The convolutions in the sclerosed portions were in some instances so markedly atrophied as to have almost disappeared from the brain surface. In most instances, however, they showed fairly well. The outermost portions of these convolutions were of diminished consistence, the underlying brain substance being unusually firm and dense.

The purport of this paper is particularly to discuss some of the conditions presented by the nervous elements of the cortex in both the atrophied and unatrophied areas. Before beginning this study, however, some considerations in regard to the normal nerve cell will not be out of place.*

* The methods used in these investigations were the methylene blue processes, particularly the one described by Nissl. Besides this the brain was also stained and studied in the fresh state (Bevan Lewis) as well as after having been hardened in the usual way. For the most part, however, the methylene blue processes will be the only ones considered.



At the outset, then, what may we consider a normal nerve cell, and in what does it consist? This brings us face to face with the problems of so much importance at the present time — those of rest and fatigue and their bearing upon the nerve cell. We shall consider a nerve cell normal which has not been subjected to diseased conditions, such as insanity, acute disease, long-continued wasting disease, disturbance of cerebral circulation or pressure. This leaves out of account then the subject of normal physiological fatigue, and we may pass to the next part of the question, namely: In what does the normal nerve consist?

In Fig. 1 we present two ganglion cells from the third layer of the human brain, which present, aside from possible evidence of fatigue, a normal condition. In these cells the nucleus remains absolutely unstained by mythelene blue and perfectly regular in outline, while the nucleolus stands out prominently near the central portion as a regularly rounded, deeply-stained body. The body of the cell is covered rather irregularly with deeply-stained masses, some of a spindle shape, others irregular in outline, and many of which show a tendency to gather in the peripheral portion of the cell body. The outline of the cell is perfectly clear and distinct in every instance, and the processes, as far as they can be traced, show these spindle-shaped masses. In Fig. 2 are shown several cells from the second layer which present a similar condition. In these cells, however, the granules of chromatin are none of them spindle-shaped, and they show a marked tendency to remain about the nucleus, and in every instance we find a clump of granules on the circumference of the nucleus and in the larger process of the cell. The nucleolus of these cells is often situated eccentrically. These, then, we will consider normal nerve cells, and I may add that the drawings were made from sections of the brain of a man in health who was killed accidentally. He lived six hours after the accident, but was entirely unconscious. The autopsy was done eight hour after death and the brain tissue was immediately placed in absolute alcohol. The nerve cells, no doubt, show evidence of fatigue, in that the granules of chromatin show such a marked tendency to gather in the peripheral portion of the cell in the large ganglion cells, and are so much scattered about the circumference of the nucleus in the small cells. The fatigue, however, did not reach beyond the physiological limit.

We may now quite consistently pass to a consideration of the case in hand.

In sections from the non-sclerosed areas stained in the fresh state the nerve cells were not only seen to be apparently diminished in number, but the outline of almost every cell was very irregular and the nucleus was very deeply stained. Vacuoles in the protoplasm of the nerve cell were very common, and almost every cell presented an extensive deposit of pigment, while free pigment granules were scattered promiscuously through the section. In the sclerosed areas these conditions were far more pronounced. Here the deposits of pigment reached the extreme degree, the number of the nerve cells were greatly reduced, and the few that remained gave evidence of disease. Scattered throughout the cortex were an immense number of bright shining droplets of colloid material.

Stained after Nissl the nerve cell presented some unusual appearances. In nearly all of the cells the granules of chromatin, when present, were scattered into the peripheral portion of the body of the cell, leaving the central portion entirely clear; in addition to this change these granules were often reduced to a dust-like consistence. This condition is fairly shown in Fig. 3. Here the granules of chromatin are not only scattered into the peripheral portion of the cell, but large portions are apparently breaking down, and so impart a homogeneous coloring to a considerable portion of the body of the cell. This condition was quite frequent. The staining of the nucleus some degree of blue was a condition almost universal. The stain varied from the deep color which I have endeavored to present in Fig. 4 to the more light shades presented in the other figures. In Fig. 4 the nucleus is not only deeply stained, but we find the cell almost entirely devoid of anything we can call granules of chromatin, and the nucleus very irregular in outline. Besides this, there is an undoubted dilatation of the pericellular lymph space which is shown in the figure.

In very many of the cells no chromatin granules were visible; in others a small amount of chromatin was to be seen scattered about the cells in fine particles, being mostly confined to the peripheral portion of the cell body. This condition is presented in Fig. 5. In one of these cells (a) we have an entire absence of chromatin; in the other (b) it is possible to distinguish some slight chromogenic areas in the peripheral portion. Cells of this character present an extremely granular cell body and a nucleus which is usually a little more deeply stained than the body of the cell.

Irregularities in the outline of the nucleus of greater or lesser degree were very common, but the most striking examples of this

condition were shown in the sclerosed areas. Here were found cells the nuclei of which presented the appearance shown in Fig. 6. In these instances the nuclei were not distorted and twisted out of shape, as is so often the case in the degenerated nerve cell, but on one side showed the irregular indentations presented in the figure, which quite reminded one of the outline drawings of the nucleus as presented by Hodge in his study of the nerve cell during electrical stimulation.* This condition of the nucleus was by no means rare, and whether or not it would indicate a subjection of the nerve cell to some powerful stimulus is a question. I have not seen exactly this condition in any other case.

Another condition which was by no means infrequent was the absence of the nucleolus from the nucleus. When this condition was found the entire absence of chromatin from the cell was the rule and the nucleus itself was but faintly outlined (Fig. 7 b). In a few of these cells, stained particles which might have been a portion of the nucleolus at some time were visible, but for the most part even these were absent. Another condition of the nucleolus (probably a preliminary stage of the one just described) is shown in Fig. 7 a. Here we have a nucleolus of very irregular contour occurring in a nerve cell entirely devoid of granules of chromatin. This condition was quite frequent and suggests the ultimate fragmentation of the nucleolus.

The last stage in the degenerative process seems to be the disappearance of the nucleus from the body of the cell. This is apparently accomplished in a gradual manner, the nucleus first swelling so as to occupy a large portion of the cell body, then becoming very granular and faint in outline, its final dissolution being coincident with that of the body of the cell itself. One stage of this degenerative process (swelling and granular condition of the nucleus) is shown in Fig. 8.

Some incidents in nerve cell degeneration remain to be described.

In large numbers of cells there was in the region of the nucleus an unstained area which varied considerably in extent. In most instances it consisted of nothing more than a slight ring about the nucleus, in some instances so marked, however, that the nucleus appeared as if cleaved from the protoplasm of the cell. The most pronounced examples of this condition were found in cells from which the chromatin had entirely disappeared. Fig. 5 a shows this condition.

* Journal of Morphology, September, 1894.

Another point of some interest was the poorly defined nuclear outline which presented itself in some of the cells. This condition was by no means confined to the more pronounced degrees of degeneration, as it occasionally presented itself in cells which were apparently in the first stages of degenerative change. An attempt is made to show this condition in Fig. 5 b; also in Fig. 3. In these the nuclear outline is hidden at various points and not very prominent in any portion. These cells present well-marked evidence of degeneration. The rare occurrence of the apparent absence of the nucleus from a cell in which the granules of chromatin are not entirely destroyed is shown in Fig. 3 b. It is quite possible that our inability to discover the nucleus in these instances is due to the excessive homogeneous staining of the entire cell. On the other hand it is not improbable that the nucleus and nucleolus may occasionally disappear from the cell before the chromatin in the cell body is entirely destroyed. I think, however, this is very unusual.

From a careful study of the nervous elements of the cortex in a case of this sort, we should be able to glean something of the life history of the nerve cell. In the foregoing description I have described the various degenerative stages in the order in which I believe they occur. Some reasons for my conclusions may not be amiss.

The more marked degrees of staining of the nucleus occur in those cells in which there is some evidence of change in the chromogenic bodies. In the more decided degrees of nuclear stain we invariably find the chromatin in a cloudy condition, its dissolution contributing undoubtedly to the coloring of the nucleus. This condition continues till the nerve cell presents the appearance shown in Fig. 4, in which the chromatin seems nearly dissolved from the cell, but the nucleus still remains stained. I have never yet seen a deeply stained nucleus in a cell where the chromatin was entirely dissolved out, and this makes the conclusion inevitable that as the chromatin disappears from the body of the cell the source from which the nucleus derives its stain is exhausted and it soon begins to fade. The washing out of the cell in the lymph stream now becomes complete, and we have the appearance presented in Fig. 5 a.

Exactly what becomes of the nucleolus is perhaps a question. Its disappearance from the nucleus is undoubted, but the manner of its going is not quite clear. From these studies I am inclined to the opinion that we have first irregularities of outline like those

presented in Fig. 7 a, then fragmentation, and finally its complete obliteration from the nucleus.

The degenerative changes in the nucleus complete the chain of destruction. This portion of the cell first becomes irregular in outline, subsequently swelling till it occupies an abnormal proportion of the body of the cell (Fig. 8). The nucleus, as well as the surrounding protoplasm, now becomes exceedingly granular, and presents such a degenerate appearance that we are forced to the conclusion that the final complete dissolution of the cell, as such, is inevitable.

Thus we have traced the life history of the nerve cell as presented by the method of Nissl. It will be noted that very little has been said about cellular vacuolation in this study. That is because the method of Nissl shows this condition but very poorly, and as we were dealing with the behavior of the nerve cell under the Nissl stain, we thought best to leave this incident in the degenerative process out of account. It may not be amiss to say, however, that the extreme degrees of vacuolation were found in the sections stained in the fresh state.

My thanks are due to Dr. P. S. Mallon for valuable assistance in making the drawings, and to Dr. H. C. Crosby of Brooklyn for aid in procuring the specimens of normal brain.

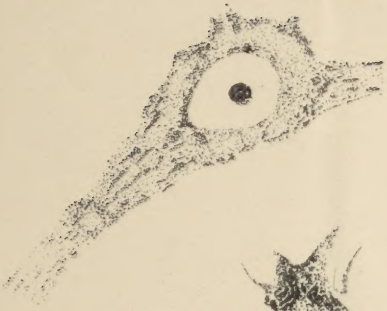


Fig. 1.

Fig. 2.

Fig. 3

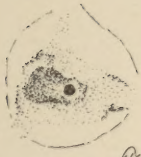


Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig 8

EXPLANATION OF PLATE.

Fig. 1. Normal nerve cells — third layer, frontal region.
Fig. 2. Normal nerve cells — second layer, frontal region.
Fig. 3. Destruction of chromatin. *a*. Nucleus stained. *b*. Nucleus apparently absent. (Third layer.)
Fig. 4. Chromatin nearly all destroyed. Nucleus stained and irregular. Dilated pericellular lymph space.
Fig. 5. Absence of chromatin from cells. Poorly defined nuclei.
Fig. 6. Irregular nucleus. (Sclerosed area.)
Fig. 7. Granular cells. Poorly defined nuclei. *a*. Irregular nucleolus. *b*. Absence of nucleolus.
Fig. 8. Granular cell. Swollen and granular nucleus.
All outlines made by aid of Abbe camera lucida.
Zeiss oil immersion, objective 1-12. Achromatic ocular No. 1.
Drawings all made from sections stained after Nissl.